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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,559	11/15/2001	David Botstein	P2730P1C40	5102

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EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/997,559	BOTSTEIN ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *119-126 and 129-131* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *119-126 and 129-131* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01 August 2005 has been entered.

Status of Application, Amendments and/or Claims

The amendment filed 01 August 2005 has been entered in full. Claims 127 and 128 are cancelled. Claims 119-126 and 129-131 are under examination.

The Audrey Goddard Declaration under 37 CFR 1.132 filed 01 August 2005 has been entered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 101 and 112, First Paragraph

Claims 119-126 and 129-131 remain rejected under 35 U.S.C. § 101 because the claimed invention is not supported by a specific and substantial asserted utility or a well established utility.

Claims 119-126 and 129-131 remain rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would clearly not know how to use the claimed invention.

The basis for these rejections is set forth at pages 3-7 of the previous Office Action (17 September 2004).

Applicant cites case law and the Utility Examination Guidelines. Applicant submits that there is a positive correlation for lung cancer and the gene encoding PRO1187 based on the gene amplification data. Applicant discusses Example 170 in the instant specification. Applicant argues that 2.25 fold to 2.928 fold amplification in squamous cell carcinomas of lung would be considered significant and credible by one skilled in the art, based upon the facts disclosed in the Goddard Declaration. As in the previous Office Action, Applicant criticizes the Examiner's reliance on Haynes *et al.,* Pennica *et al.* and Konopka *et al.* (all of record). Applicant argues that the cited art does not support the teaching that nucleic acid copy number is not predictive of a similar association for protein in general. As in the previous Office Action, Applicant discusses their submitted references (Orntoft *et al.*, Hyman *et al.* and Pollack *et al.* all of record) to demonstrate that when a gene is amplified in cancer, it is more likely than not that the encoded protein will be expressed at an elevated level.

Applicant's arguments have been fully considered but are not found to be persuasive. The Declaration by Dr. Goddard has been fully considered but is not deemed persuasive. The PRO1187 gene has *not* been associated with tumor formation

or the development of cancer, nor has it been shown to be predictive of such. The specification demonstrates that the PRO1187 nucleic acid was amplified in some cancers. Thus, it is not known **whether PRO1187 is expressed** in corresponding normal tissues, and what the relative levels of expression are (Emphasis added). In the absence of any of the above information, all that the specification does is present evidence that **the DNA encoding PRO1187 is amplified** in a variety of samples and invites the artisan to determine the significance of this increase (Emphasis added). Pennica *et al.* was cited as evidence showing a lack of correlation between gene (DNA) amplification and elevated mRNA levels. Konopka *et al.* was cited as evidence showing lack of correlation between gene amplification and increased protein levels. Haynes *et al.* was cited as providing evidence that protein levels cannot be accurately predicted from mRNA levels, and that variances as much as **40-fold** or even **50-fold** were not uncommon (p. 1863).

Applicant argues that even if there were no correlation between gene amplification and increased mRNA/protein expression, a polypeptide encoded by an amplified gene in cancer would still have utility and provide information for cancer diagnosis and treatment. Applicant cites the 1.132 Declarations of Ashkenazi and Polakis (of record). Applicant discusses the reference of Hanna and Mornin (of record). Applicant contends that one of skill in the art would reasonably expect based on the gene amplification data for the PRO1187 gene, the declarations submitted and the articles presented, that the PRO1187 polypeptide is most likely overexpressed in certain

lung tumors, just like the PRO1187 gene, and is therefore useful as a tumor marker for certain lung cancers.

None of the articles submitted by Applicant, teach that the research was relevant to identifying probes that can be used as cancer diagnostics. Furthermore, there is no evidence regarding whether or not the **PRO1187 mRNA or protein levels** are also increased in these tumor samples (Emphasis added). The state of the art regarding gene amplification and increased protein levels can be opposing as indicated by the references cited by the Examiner and Applicant. Indeed, given the disclosure in art, such as Pennica *et al.*, Konopka *et al.*, and Haynes *et al.*, that there is not always such a correlation, the skilled artisan would not assume it is so, **but would perform the experiment to verify it** (Emphasis added). It is noted that the literature cautions researchers from drawing conclusions based on small changes in transcript expression levels between normal and cancerous tissue. For example, Hu *et al.* (2003, Journal of Proteome Research 2:405-412) analyzed 2286 genes that showed a greater than 1-fold difference in mean expression level between breast cancer samples and normal samples in a microarray (p. 408, middle of right column). Hu *et al.* discovered that, for genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a strong and significant correlation between expression level and a published role in the disease (see discussion section). Since the instant claims are directed to the PRO1187 protein (SEQ ID NO:399), it was imperative to find evidence in the relevant

scientific literature whether or not a small increase in DNA copy number would be considered by the skilled artisan to be predictive of increased mRNA and protein levels.

The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Applicant incorporates their response to the rejection under 35 USC 101 in response to the rejection under 35 USC 112, first paragraph. Applicants arguments have been fully considered but are not found to persuasive for the reasons discussed above in the maintained rejection in 35 USC 101.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

Claims 119-123 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification provides adequate written description for SEQ ID NO:399, but not variants.

The claims are drawn to an isolated native sequence polypeptide having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence and a specific activity. The instant specification contemplates but does not exemplify variants of the protein wherein the variant can have any number of substitutions, deletions, insertions and/or additions in SEQ ID NO:399, wherein said nucleic acid

encoding said polypeptide is amplified in squamous cell carcinomas of lung. The specification does not provide any guidance as to what changes should be made and which regions of the instant protein are functionally and structurally critical. There is no description of variants of SEQ ID NO:399 that exist, while still maintaining function. There is no identification of any particular portion of the structure that must be conserved in order to conserve the required function.

The disclosure fails to describe the common attributes or characteristics that identify the members of the genus. The genus is highly variant because a significant number of structural differences between genus members are permitted. Thus, SEQ ID NO:399 alone is insufficient to describe the genus. The disclosure fails to provide a representative number of species to describe the genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of

isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO:399, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JOSEPH MURPHY
PATENT EXAMINER

RMD
10/3/05